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Understanding Pediatric Hemoglobinopathies: Epidemiology, Genetics, and Management Strategies

Amjad Jamil Abu-Sharar[1*], Nader Faris Zayadeen[2], Amani Suleiman Almanasrah[3]

[1]Primary Health Care Corporation-Qatar
[2]Primary Health Care Corporation-Qatar
[3]Ophthalmology Specialist at PHCC-Qatar

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***Corresponding author:** Amjad Jamil Abu-Sharar
Primary Health Care Corporation-Qatar

Abstract **Review Article**

Children's hemoglobinopathies, such as thalassemias and sickle cell disease (SCD), present a diverse range of symptoms and complex genetic causes, which provide significant challenges for therapy. This website provides comprehensive information on the genetics, prevalence, and many treatment options available for baby hemoglobinopathies. Research in global epidemiology suggests that individuals suffer from a diverse array of ailments. Therefore, it is crucial to prioritize targeted screening programs and medicines. Understanding the fundamental concepts of basic genetics, such as autosomal recessive inheritance patterns and specific gene mutations, is crucial for developing precise diagnostic tools and personalized treatment strategies. Comprehensive management strategies encompass several approaches such as providing supportive care, utilizing pharmaceutical therapy, and implementing advanced techniques like gene therapy for treating disorders. Due to continuous research that enhances our comprehension of hemoglobinopathies, we should expect improved results and an enhanced standard of living for individuals affected by them. The purpose of this study is to enhance our comprehension of pediatric hemoglobinopathies and our approach to therapy by gathering the perspectives of epidemiology, genetics, and clinical practice.

Keywords: Pediatric hemoglobinopathies, Sickle cell disease (SCD), Thalassemia, Epidemiology, Genetics.

INTRODUCTION

Hemoglobinopathies, such as sickle cell disease (SCD) and thalassemia, have significant consequences for the overall health of children, especially in places where they are common (Ahmed *et al.,* 2024). These genetic flaws that hinder the production of hemoglobin cause various challenges for individuals affected by these illnesses, as well as their families and the healthcare system as a whole (Kar *et al.,* 2024). In order to achieve effective interventions and achieve better outcomes, it is crucial to understand the interaction between therapy options for pediatric hemoglobinopathies, genetics, and epidemiology (Angastiniotis, 2024).

The regional and ethnic distribution of sickle cell disease and thalassemia varies. Specifically, the regions of South Asia, Africa, the Mediterranean, and the Middle East have the highest number of individuals affected by SCD (Badr *et al.,* 2024). Roughly 75% of infants with sickle cell disease (SCD) are born in Sub-Saharan Africa, which exerts a significant burden on the healthcare system of the region (Bell *et al.,* 2024). Thalassemia is more commonly found in the Mediterranean basin, the Middle East, Southeast Asia, and specific areas of the Indian peninsula. The regional differences emphasize the importance of tailoring healthcare interventions and resource allocation to meet the individual needs of impacted areas (Hossain *et al.,* 2024). Children with hemoglobinopathies commonly have genetic diseases that specifically impact the components of hemoglobin. In sickle cell disease (SCD), the beta-globin genes are usually the ones affected, while in thalassemia, both the alpha and beta globin genes are affected (Inusa *et al.,* 2024). Genetic abnormalities that impact the synthesis, operation, or arrangement of hemoglobin are accountable for the distinct characteristics of each illness. Carrier screening, genetic counseling, and prenatal testing are essential for persons at risk due to the intricate nature of disease transmission processes and the gravity of their effects (Mensah *et al.,* 2021).

Managing pediatric hemoglobinopathies involves addressing symptoms, preventing complications, and enhancing overall health outcomes (Obeagu *et al.*,2024). There are two types of interventions: early baby screening programs and comprehensive multidisciplinary care teams. Furthermore, they encompass educational programs, disease-modifying medications, supportive care methods, and continuing research projects (Olney *et al.*, 2023). Gene therapy and stem cell transplantation are promising procedures that have the potential to significantly transform disease treatment (Raghuraman *et al.*, 2024). As an understanding of these methods grows, they offer hope for the creation of novel therapeutic alternatives (Mekelenkamp *et al.*, 2024).

The resolution of the complex issues related to pediatric hemoglobinopathies requires the cooperation of healthcare professionals, researchers, policymakers, and community members. To ensure a better and happier future for children with hemoglobinopathies, it is crucial for everyone to come together and actively promote the spread of knowledge, improve access to healthcare, and enhance understanding of the scientific principles involved (Rodigari *et al.*, 2024).

Epidemiology:

Hemoglobinopathies, such as sickle cell disease (SCD) and thalassemia, have a significant impact on children's health. These conditions highlight the importance of genetic, socioeconomic, and geographical factors in determining the prevalence and consequences of the diseases (Bell *et al.*, 2024). Regions with a high incidence of malaria, such as Sub-Saharan Africa, the Middle East, and some parts of India, have traditionally had a greater occurrence of sickle cell disease (SCD) (Rajput *et al.*, 2024). The regional distribution is a direct consequence of the evolutionary adaptation to malaria, rather than being a random occurrence. Heterozygotes, individuals with one copy of the sickle cell gene, have a higher level of adaptation to malaria-prone areas because they are less likely to get sick (Depetris-Chauvin and Weil, 2018). However, offspring of carriers face a 25% higher likelihood of getting sickle cell disease (SCD) since they will inherit two copies of the faulty gene (Morgan *et al.*, 2024).

Thalassemia shows variations in prevalence in different regions around the world. Intra-familial marriage is most common in the Mediterranean region, South Asia, specific areas of the Middle East, and Southeast Asia (Kattamis *et al.*, 2020). The occurrence of severe types of thalassemia is higher among individuals from these families who marry within the family, as this raises the probability of inheriting two faulty genes from both parents (Ramadianti *et al.*, 2024). Despite the progress made in medical treatment and preventive measures, juvenile hemoglobinopathies still have a devastating impact on affected children and their communities (Di Paola *et al.*, 2024). Some areas have very high rates of occurrence, emphasizing the importance of developing specific public health measures including neonatal screening programs, genetic counseling services, and easy access to specialized healthcare facilities (Knapkova *et al.*, 2018).

The frequency of pediatric hemoglobinopathy is significantly influenced by discrepancies in healthcare access and funding, particularly in low-income and middle-income nations (Panchbudhe *et al.*, 2024). Children living in these areas experience higher rates of death and disease because they do not have access to fundamental medical interventions such prenatal diagnosis, comprehensive illness treatment, and early intervention (Delaney and Smith, 2012). In addition, families of children with hemoglobinopathies face additional difficulties such as insufficient healthcare infrastructure, poverty, and restricted access to information. These obstacles are further compounded by the fact that they live in various geographical regions (Phillips *et al.*, 2022). Thalassemia and sickle cell disease (SCD) are enduring ailments that can impose economic burden on families. This could lead to reduced employment, heightened costs, and a deterioration in general quality of life (Windermere and Nunn, 2024). Given the intricate nature of pediatric hemoglobinopathies from an epidemiological standpoint, a comprehensive approach is necessary, encompassing community engagement, implementation of public health initiatives, and collaboration on a global scale (Inusa *et al.*, 2024). To decrease the worldwide occurrence of these severe genetic disorders and enhance the well-being of affected children and families, we can achieve this by spreading knowledge, ensuring availability of essential healthcare, and offering financial backing for research and inventive methods (Halim-Fikri *et al.*, 2022).

Genetic Basis:

Thalassemia and sickle cell disease (SCD) are two pediatric hemoglobinopathies caused by genetic abnormalities in the genes that produce hemoglobin proteins (Gupta *et al.*, 2024). Red blood cells possess hemoglobin, a molecule that enables the transportation of oxygen from the lungs to all tissues in the body (Selvan *et al.*, 2024). Hemoglobin consists of four protein chains: two alpha globin chains and two beta globin chains (Kazem *et al.*, 2024). Problems in the production of hemoglobin can lead to the appearance of symptoms associated with sickle cell disease (SCD) and thalassemia. This can happen if the genes responsible for encoding these globin chains experience a failure (Raghuraman *et al.*, 2024).

The presence of a point mutation in the HBB gene, which is situated on chromosome 11, is the primary cause of sickle cell disease. This gene is responsible for encoding the subunit of hemoglobin known as beta globin (Traeger-Synodinos *et al.*, 2024). The sixth codon of the HBB gene undergoes a substitution of adenine

with thymine, leading to the creation of hemoglobin S (HbS), which is an unfavorable variation of hemoglobin (Macharia *et al.,* 2024). Hemoglobin S is more prone to polymerization than hemoglobin A in low oxygen conditions. This leads to the creation of red blood cells that have a sickle shape. The presence of these inflexible, curved cells can impede the circulation of blood, leading to harm to tissues, episodes of blood vessel blockage, and other medical difficulties (Elendu *et al.,* 2023).

Thalassemia is a term used to describe a collection of hereditary illnesses where the body produces a limited or nonexistent amount of beta or alpha globin chains (Begum *et al.,* 2024). Alpha thalassemia occurs when there is a deletion or alteration in one or more of the four alpha globin genes found on chromosome 16 (Musallam *et al.,* 2024). Plasmodium alpha thalassemia can present in two more severe variants when there is a deletion of several alpha globin genes (Kaur *et al.,* 2024). The two disorders are hemoglobin H disease and hydrops fetalis (Amid *et al.,* 2024). Nevertheless, beta thalassemia is caused by genetic abnormalities in the HBB gene, which is also responsible for the development of sickle cell disease (Poonam *et al.,* 2024). On the other hand, beta thalassemia is caused by many mutations that occur in the beta globin gene (Mamata *et al.,* 2024). Unlike sickle cell disease (SCD), which is caused by a single point mutation resulting in faulty hemoglobin synthesis, this condition is different. Genetic changes can hinder the formation of alpha and beta globin chains, leading to beta thalassemia or a decrease in production (Inusa *et al.,* 2019). This can lead to the formation of solid crystals made up of unbound alpha globin chains, which can cause damage to cells and decrease the effectiveness of erythropoiesis (Zhuang *et al.,* 2023). The symptoms of sickle cell disease (SCD) and thalassemia are affected by various causes, such as environmental effects, genetic factors that might modify DNA, and hereditary genetic mutations (Zahed, 2023). Sickle cell disease (SCD) presents with a range of symptoms, from carriers who show no symptoms to individuals who frequently face life-threatening disorders such as vaso-occlusive crises, acute chest syndrome, strokes, and other complications (Bhawnani and Yadav, 2023).

Thalassemia presents with a wide range of clinical symptoms, ranging from those who show no symptoms but carry the condition, to severe cases that require regular blood transfusions and iron chelation therapy to manage problems such as organ damage, excessive iron levels, and anemia (Pinto *et al.,* 2020).

Understanding the basic genetic pathways that cause pediatric hemoglobinopathies is crucial for accurate diagnosis, genetic counseling, and the creation of specific therapeutic strategies that relieve symptoms, prevent complications, and enhance the quality of life for affected individuals (Karamperis *et al.,* 2021). The progress of next-generation sequencing technologies, along with improvements in molecular genetics, has made it easier to discover new genetic modifiers and potential targets for treatment (Wang *et al.,* 2023). Consequently, there is a sense of hopefulness regarding enhanced treatment results and customized strategies for handling these difficult conditions (Kalariya *et al.,* 2023).

Management Strategies:

Efficient management of children suffering from hemoglobinopathies, such as sickle cell disease (SCD) and thalassemia, requires the use of a comprehensive approach that takes into account the specific needs of each patient and the various ways in which their symptoms may appear (Kunz and Kulozik, 2020). Various therapy methods are used to improve results and promote the well-being of teenage patients and their families (Berry *et al.,* 2023). These encompass preventive strategies, supportive care interventions, disease-modifying drugs, and early identification (Sabbagh *et al.,* 2020).

Effective treatment of children with hemoglobinopathies requires collaboration among teams of multidisciplinary care, including hematologists, physicians, genetic counselors, nurses, social workers, psychologists, and other allied health professionals (Ferreira *et al.,* 2012). The utilization of a team-based approach in this treatment method ensures that patients and their families receive a thorough and personalized therapeutic experience. Each person brings their own expertise and skills to help with the complex care of hemoglobinopathy, including medical, psychological, and educational elements (Phillips *et al.,* 2022).

Programs aimed at promptly diagnosing hemoglobinopathies in newborns are crucial in order to ensure that affected children promptly receive the necessary treatment (Galadanci *et al.,* 2024). Effective screening tests can detect newborns who are at risk of developing sickle cell disease (SCD) or thalassemia by assessing dangerous hemoglobin variations or genetic mutations (Runkel *et al.,* 2020). These operations are commonly carried out quickly after the baby is born (Runkel *et al.,* 2020). Timely diagnosis allows doctors to start therapies that improve outcomes, inform families about the condition, and put preventive measures into action (Angastiniotis *et al.,* 2024).

Disease-modifying medications have demonstrated efficacy in relieving symptoms, preventing complications, and enhancing the general well-being of children with hemoglobinopathies (Mkwambe *et al.,* 2024). Hydroxyurea is the primary medicine used to treat sickle cell disease. It elevates the levels of fetal hemoglobin, which in turn decreases the occurrence and intensity of vaso-occlusive crises and associated problems (Mkwambe *et al.,* 2024). Hematopoietic stem cell transplantation (HSCT) involves the replacement of damaged hematopoietic cells with healthy donor cells.

Occasionally, this has the potential to provide a cure for patients who are severely ill (Casirati *et al.*, 2023).

The goal of treating asymptomatic patients is to relieve acute symptoms, prevent complications, and enhance the patient's overall health. Aside from non-pharmaceutical interventions like heat therapy and massage, pain management can involve the use of painkillers such as opioids and nonsteroidal anti-inflammatory drugs (NSAIDs) (Mayoral *et al.*, 2022). Medication can be effective in treating infections, but patients who have severe anemia may need to have regular blood transfusions in order to maintain optimal health and prevent complications including stroke and organ damage (Fortin *et al.*, 2018).

Supportive Care refers to the provision of services that address the physical, mental, and social needs of children and their families. In order to achieve the best possible growth and development, it is recommended that persons incorporate folic acid and other vitamin supplements into their diet, while maintaining proper hydration by drinking ample amounts of water (Farmakis *et al.*, 2021). Children with impaired immune systems are more resistant to becoming ill if they receive vaccines for infectious diseases. Healthcare practitioners has the capacity to identify and tackle problems at an early stage through the regular evaluation of organ function, growth, and development (Pittet *et al.*, 2021). Education for the patient and their families is a crucial aspect of providing comprehensive care for children with hemoglobinopathies. Education programs impart knowledge to individuals about the genetic basis of the condition, its clinical symptoms, possible treatments, symptom control, and preventive actions (Gülleroğlu *et al.*, 2007). Genetic counseling aids individuals in making informed decisions regarding conception, childbirth, and the inheritance of traits (Singh *et al.*, 2024). Support groups and individual therapy are two types of psychosocial support services that can help children and families with hemoglobinopathies cope with the emotional and social difficulties they encounter (Drahos *et al.*, 2024).

Ongoing research in the field of juvenile hemoglobinopathies is leading to advancements in the management of these conditions (Almashjary, 2024). The goal is to develop new therapeutic strategies and enhance overall prognoses (Almashjary, 2024). The progress in gene editing and gene therapy shows promise in correcting the genetic abnormalities responsible for thalassemia and sickle cell disease (SCD), which could lead to the creation of effective treatments (Dimitrievska *et al.*, 2024). Pharmaceutical interventions, such as gene-based therapies, targeted drugs, and supportive care measures, are subjected to thorough clinical testing to determine their effectiveness and safety (Dănilă *et al.*, 2024). Collaborative research efforts including academic institutions, corporate partners, and patient advocacy groups are being undertaken to enhance the well-being of children and families afflicted by these intricate genetic illnesses (Drahos *et al.*, 2024). These attempts aim to accelerate the application of scientific breakthroughs.

CONCLUSIONS

Pediatric hemoglobinopathies are a group of complicated genetic diseases that have big effects on public health and treatment methods. By explaining the genetics, how these disorders are spread, and treatment choices, doctors can better understand these conditions and provide better care to patients and their families. For kids with juvenile hemoglobinopathies to have better treatment choices and a better quality of life overall, research and new ideas must keep coming up.

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